LISTING OF THE CLAIMS

Claim 1 **(currently amended)** A method for the production of a ~~VHH~~ single heavy chain antibody in a non-human mammal comprising the step of expressing a heterologous VHH heavy chain locus in that mammal specifically in B cells in response to antigen challenge.

Claim 2 **(currently amended)** A method according to claim 1 wherein the VHH heavy chain locus comprises:

(a) at least one VHH region each comprising one VHH exon, at least one D region each comprising one D exon and at least one J region each comprising one J exon, wherein the VHH region, the D region and the J region are capable of recombining to form VDJ coding sequence,

(b) a constant heavy chain region comprising at least one ~~Cγ~~ constant heavy chain gene, ~~and which when expressed~~ wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain ~~nor a functional CH4 domain~~,

~~(c) a recombination sequence (rss) capable of recombining a J region of step (a) directly with a Cγ constant heavy chain gene of step (b),~~

and which locus when expressed ~~is capable of forming a~~ leads to the formation of a single heavy chain antibody ~~IgG molecule (scIgG)~~.

Claim 3 **(currently amended)** A method for the production of a ~~camelised VH~~ single heavy chain antibody in a non-human mammal comprising the step of expressing a camelised VH heavy chain locus in that mammal specifically in B cells in response to antigen challenge.

Claim 4 **(currently amended)** A method according to claim 3 wherein the camelised VH heavy chain locus comprises:

(a) at least one VH region each comprising one VH exon which is mutated such that ~~the nucleic acid sequence is the same as a camelid VH exon~~ , when expressed, the resulting single heavy chain antibody is stabilised [[("camelised VH exon")]], at least one D region each comprising one D exon and at least one J region comprising one J exon, wherein the VH region, the D region and the J region are capable of recombining to form VDJ coding sequence, and

(b) a constant heavy chain region comprising at least one ~~Cγ~~ constant heavy chain gene, ~~and which when expressed~~ wherein each of said at least one constant heavy chain gene, when expressed, does not express a functional CH1 domain ~~nor a functional CH4 domain~~,

~~(c) a recombination sequence (rss) capable of recombining a J region of step (a) directly with a Cγ constant heavy chain gene of step (b),~~

and which locus when expressed ~~is capable of forming a complete~~ leads to the formation of a single heavy chain antibody ~~IgG molecule (scIgG)~~.

Claims 5 – 6 **(canceled)**

Claim 7 **(currently amended)** A method according to claim 1 or 2 wherein the VHH single heavy chain locus comprises a camelid VHH, at least one D region of human origin and at least one J region of human origin and a constant region of human origin.

Claim 8 **(currently amended)** A method according to claim 3 or 4 wherein the camelised VH heavy chain locus comprises at least one D region of human origin and at least one J region of human origin and a constant region of human origin.

Claim 9 **(canceled)**

Claim 10 **(currently amended)** A method according to claim 1 or 3 wherein the constant heavy chain region comprises at least one constant region heavy chain gene which is of non-camelid origin.

Claim 11 **(original)** A method according to claim 10 wherein at least one constant region heavy chain gene is of human origin.

Claims 12 – 16 **(canceled)**

Claim 17 **(withdrawn)** A VHH single heavy chain antibody obtainable according to the method of claim 1 wherein that part of the antibody encoded by a VHH exon is encoded by an exon of camelid origin and the remainder of the antibody molecule are encoded by one or more regions of human origin.

Claim 18 **(withdrawn)** A VHH single heavy chain antibody obtainable according to the method of claim 1 wherein that part of the antibody encoded by a VHH exon is encoded by a exon of camelid origin and the constant heavy chain region is encoded by one or more regions of rabbit origin.

Claim 19 **(withdrawn)** A VHH single heavy chain antibody obtainable according to the method of claim 1 wherein that part of the antibody encoded by a VHH exon is encoded by a exon of camelid origin and the constant heavy chain region is encoded by one or more regions of mouse origin.

Claim 20 **(withdrawn)** A camelised VH single heavy chain antibody obtainable according to the method of claim 3.

Claim 21 **(withdrawn)** A camelised VH single heavy chain antibody according to claim 20 wherein the whole of the antibody is encoded by one or more regions of human

origin.

Claim 22 **(withdrawn)** A camelised VH single heavy chain antibody according to claim 20 wherein that part of the antibody encoding the constant heavy chain region is encoded by one or more regions of rabbit origin.

Claim 23 **(withdrawn)** A camelised VH single heavy chain antibody according to claim 20 wherein that part of the antibody encoding the constant heavy chain region is encoded by one or more regions of mouse origin.

Claim 24 **(withdrawn)** A camelised VH single heavy chain antibody according to claim 20 which is a monoclonal antibody.

Claim 25 **(withdrawn)** A vector comprising a VHH heavy chain locus described according to claim 1.

Claim 26 **(withdrawn)** A vector comprising a camelised VH heavy chain locus described according to claim 3.

Claim 27 **(withdrawn)** A host cell transformed with a vector according to claims 25.

Claim 28 **(withdrawn)** A transgenic mammal expressing a heterologous VHH heavy chain locus described according to claim 2.

Claim 29 **(withdrawn)** A transgenic mammal expressing a camelised VH heavy chain locus described according to claim 4.

Claim 30 **(withdrawn)** A transgenic mammal according to claim 28 which is a mouse.

Claim 31 **(withdrawn)** A method for the production of single chain antibodies by immunising a transgenic mammal according to claim 28 with an antigen.

Claim 32 **(withdrawn)** The use of a single heavy chain antibody according to claim 17 in the preparation of a medicament for the prophylaxis and/or treatment of disease.

Claim 33 **(new)** The method of claim 1 or 2 wherein the entire VHH single heavy chain locus is of camelid origin

Claim 34 **(new)** The method of claim 3 or 4 wherein the camelised VH single heavy chain locus is of human origin.

Claim 35 **(new)** The method of claim 3 or 4 wherein the camelised VH single heavy chain locus is of non-human origin.

Claim 36 **(new)** The method of claim 3 or 4 wherein the camelised VH single heavy chain locus is of camelid origin.

Claim 37 **(new)** The method according to claim 1 or 3 wherein the antibody is a monoclonal antibody, said method further comprising the steps of isolating the spleen from said transgenic animal, fusing said spleen cells with a myeloma to produce hybridoma cells, and isolating said antibody from said hybridoma cells.

Claim 38 **(new)** The method according to claim 1 or 3 wherein the antibody is a monoclonal antibody, said method further comprising the steps of isolating antibody-producing cells from said transgenic animal, isolating nucleic acid from said cells, utilizing said nucleic acid to prepare a phage display library, selecting phage displaying antigen specific VHH or camelised VH binding domains, and isolating said binding domains.